

Figure 1 represents compound of formula II, as described in EP 0494078, page 4 lines 1-24, and defining antibiotic GE 2270 factor A<sub>3</sub> when W is selected as COOH.

Figure 2 represents compound of formula I of the subject application.

To clarify the differences, we arbitrary numbered the heterocyclic rings of formulae II and I and we indicated with an "A" arrow the isopropyl group and with a "B" arrow the amide group, whose position, in applicants' opinion, differentiate the compounds.

As concerns compound of formula II according to EP 0494078 (Figure 1), note that the isopropyl group is positioned between rings numbered as 3 and 4, while the amide group is positioned between rings numbered as 4 and 5.

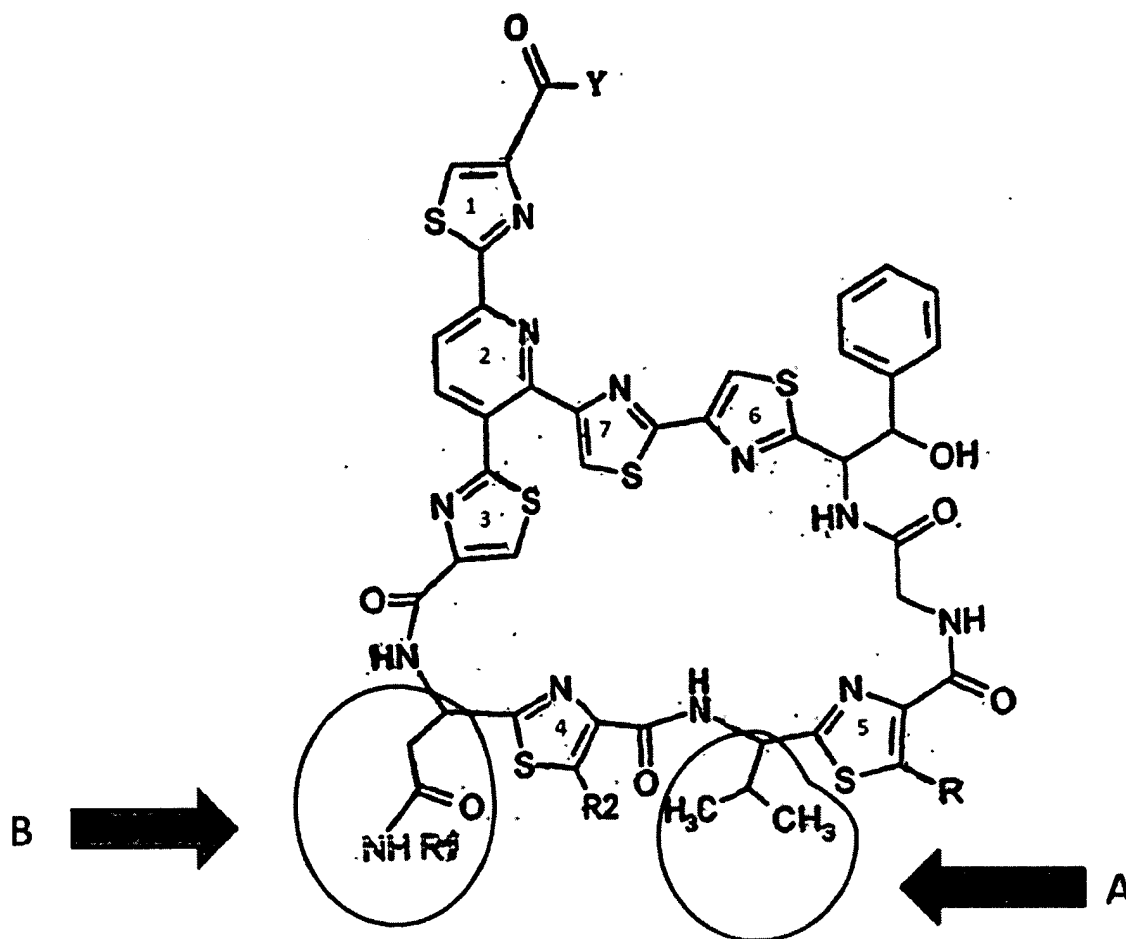
By contrast, taking into consideration the compound of formula I according to the present invention, please note that the isopropyl group is positioned between rings numbered as 4 and 5, while the amide group is positioned between rings numbered as 3 and 4. It is clear that compound of formula II (as described in EP 0494078) and compound of formula I (according to the present invention) are not the same, but are different hence there is no anticipation.

In light of these comments, EP 0494078 does not define, as antimicrobial agents that are active against gram positive and gram negative bacteria, the same compounds as those according to the present invention, and therefore novelty of the compounds of formula I according to the present invention, i.e. claims 33, 47 and 48 can be properly claimed.

Figure 1: compounds of formula II according to EP 0494078



Figure 2: compounds of formula I according to the present invention



It will also be noted that, as briefly mentioned above, EP 0494078 describes compounds that are novel amide derivatives of antibiotic GE 2270 compounds. Several antibiotics are described including for example compound 33 (Table II, page 36). Some of the selected antibiotics have antimicrobial activity against gram positive and gram negative bacteria, as shown in Table VII.

The historical definition of “antibiotic” is: “a substance produced by a microorganism which inhibits the growth of other microorganisms”. This definition has been extended to include also compounds of synthetic origin able to inhibit the growth of microorganisms. Based on the above definitions, all compounds possessing antibacterial activity can be defined as antibiotics.

However, the reverse is not necessarily true. Indeed there are several examples of compounds produced by microorganisms that have no antibacterial activity and are used for indications other than anti-infective therapy. Examples taken from among drugs in clinical use include: cyclosporine, rapamycin and tacrolimus, all antibiotics having immunosuppressive activity; lovastatin, an antibiotic having activity as cholesterol lowering agent; bleomycin, adriamycin, distamycin, mitomycin and many other antitumor agents also falling under the historical definition of “antibiotics”; acarbose, an anti diabetic compound; spinosyn, an insecticide; bialophos, an herbicide; avermectin, an anti helminthic agent, etc. Many more compounds falling under the historical definition of “antibiotic” but devoid of any antibacterial activity are currently under study for many indications. Therefore, the statement that an antibiotic is necessarily an antibacterial agent is not correct.

Thus it is well known, and therefore it is common general knowledge, that **antibiotic** is “any of a variety of substances, usually obtained from microorganisms” and it is also well known that antibiotic is not synonym of antimicrobial. In fact, in scientific literature many antibiotics with anti-inflammatory, anti-tumoral, anti-bacterial or immune suppression activity are described.

In response to the examiner’s comments in item 1), note that compound 33, as described in EP 0494078 (as well as in US 5,599,791), is an antibiotic, having similar formula with respect to compounds of formula (I) of the present application. However, the assay reported in Table VII of EP 0494078, shows the minimal inhibitory concentrations (MIC) for some microorganisms among which *Staphylococcus aureus* and *Propionibacterium acnes*, has not been carried out with compound 33.

Although not raised in the current Action, applicants’ claims are also non-obvious over the compounds of the cited documents. In view of the above, EP 0494078 does not describe nor suggest any antimicrobial activity with respect to compound 33, that can represent the closest prior art. As explained above, EP 0494078 only discloses that compound 33 has is an antibiotic, but nothing is said or suggested about any possible antimicrobial activity of this compound. In view of the fact that an antibiotic compound can show very different activities, such as for example antitumor, anti-inflammatory activity, EP 0494078 does not suggest any antimicrobial activity for compound 33.

In view of these teachings, it would be not obvious to the person skilled in the art that compound of formula (I) according to the present invention could be an anti-microbial agent.

In addition, particularly as concerns the described antimicrobial activity of some of the compounds as disclosed in EP 0494078 (but, as already said, none referring to compound 33), the following has to be noted. All the compounds described in EP 0494078 as having an antimicrobial activity, show an inhibitory activity against *S. aureus*. The teaching of EP 0494078 thus shows a kind of correlation between the anti-microbial activity and the inhibition of *S. aureus*.

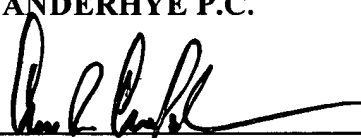
Amide derivatives according to the present invention show an antimicrobial activity but do not inhibit *S. aureus*. This is an additional reason why the skilled person would not have been induced to reach the inventive concept underlying the present invention even though he would have been aware of the teaching of EP 0494078.

For the above reasons it is respectfully submitted that claims 33, 47 and 48 define patentable subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

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